

Pre-hospital blood transfusion

- *and changes in cardiac stroke volume*

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Preface

During the spring of 2011, Major Are Langaard Jensen sent an email, on behalf of Major Erling Bekkestad Rein, to all the cadets in class Guettler. The mail contained bachelor topics related to medical issues. After graduation I will start my service in the Norwegian Armed Forces Medical Services, and that is also mainly the reason why I chose to write my bachelor's degree on a related topic. I have not been in the medical services before and would therefore enjoy having some knowledge of a relevant topic before I start working there. The topic that interested me the most was the one concerning blood transfusion and its effects on the donating part. I did not have any experience with this subject before writing this paper, but it is a very relevant topic for the medics at the time being. I have chosen to write the paper in English because it is a pilot project and the main project that will be carried out later will also be written in English. This way the pilot study will facilitate for the preliminary work pilot of the main project. Another reason is that most of the relevant theory and research made on the topic is written in this language.

I would also use this opportunity to thank the two test persons who agreed to participate in the experiment. Without their effort the experiment could not have been carried out. I would also especially like to thank Dr. Erling B. Rein for his help and guidance throughout this study. His devotion to the subject and encouraging support throughout the writing process has been invaluable.

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1. Introduction

1.1 Background

The war in Afghanistan (2001-present) has given the Norwegian Armed Forces unique combat experience. Unfortunately Norway has lost 9 soldiers, and 26 have been wounded in combat (2001-2010). For the first time, the nation has witnessed live on television soldiers returning in coffins, draped in the Norwegian flag. This has led to a change in attitude towards combat casualty care. Politicians have stated that “only the best is good enough for our soldiers”. Medevac helicopters were stationed in Afghanistan on a permanent basis. A demand for qualified surgeons in Afghanistan led to a dispute in national papers, and finally the resignation of the General Surgeon who demanded the improvement.

The main developments in Tactical Combat Casualty Care (TCCC) have originated in the USA, and most improvements have been imported to us from our Allies. The Norwegian armed forces does not have the capacity to do extensive research and development, and picking up the best from our friends and evaluating it for use within our own forces is a reasonable strategy. One of the newest and most interesting improvements is the use of fresh whole blood (FWB) far forward. Far forward in this setting can be defined as pre-hospital, this means before the casualty is treated by a surgeon (Role 3 facility).

1.2 Why is the topic relevant?

The leading cause of death on the battlefield is uncontrolled haemorrhage (60%), and more than two thirds of these deaths are caused by non-compressible haemorrhage (Bellamy, 1984). Non-compressible haemorrhage is located to the abdomen and/or thorax (together called truncus) and is much more difficult to control. Since there is no way of compressing the arteries against a firm structure, packing the wound with compresses is the only option (Butler et.al. 2007). These patients represent a group of casualties that is potentially salvageable (Kotwal et.al, 2011). The current treatment of truncal haemorrhage is called

hypotensive resuscitation. This means that the patient will be allowed to temporarily have a lower blood pressure, typically systolic 70-90 mmHg (Dawes et.al, 2009). This reduces bleeding, while perfusion to the brain is adequate. No intravenous fluids must be given (Haut et.al, 2011). The only liquid that can be used for resuscitation is then blood. Blood has oxygen carrying capacity and hemostatic function, and is thus perfect for this use. There is only one problem: how to logistically bring blood forward?

In this paper I will describe what buddy transfusion is, and how this can solve this logistical challenge. I will further discuss the feasibility of buddy transfusion in the military setting, with a focus on safety of the donors. Finally I will look into one of the physiological challenges: does buddy transfusion immediately change the volume of blood pumped out by the heart? Especially the stroke volume (SV) since this is correlated with internal haemorrhage from combat wounds. I have also conducted a small pilot study. To my knowledge, there has not been any testing of the effects on SV immediately after donating blood. Most experiments have directed their focus towards carrying out tests 24 hours after the blood has been donated. What this implies is that there is little, if any knowledge about the donor safety aspects immediately after donation. The immediate effects are very interesting since any donor can be expected to return to combat immediately after blood donation. The effects on the donating part's SV have not yet been explored. This is why my experiment will attempt to "explore changes in stroke volume during graded exercise before and immediately after donation of one unit (450 ml) of blood. In addition to exploring the changes in stroke volume, I will discuss what (safety) aspects will be relevant if we introduce buddy transfusion primarily to the Special operations forces during international operations"?

2. Theory

Key words: blood, whole blood, buddy transfusion, stroke volume, physical requirements.

2.1 Introduction to the theoretic part

The following chapter will give an account of the relevant theory for this paper. I will first explain the principle of the use of blood and blood transfusion and point out the challenges of blood logistics in the field. Then I will explain the concept of buddy transfusion and its limitations. I will also give an account of how the human body reacts to exercise. In addition to the above, I will write about the practices when donating blood and the physical requirements a soldier is met with today. Finally I will give the theoretical background for the pilot study that was done as a part of this paper.

2.1.1 Blood and blood transfusion

Surgery and the transfusion of blood is the main treatment for non-compressible haemorrhage (Remick et.al, 2010). Traditionally, because of the logistical challenges, blood has not been available for pre-hospital care, and intravenous fluids have been used instead. The reason for this can be found in how modern blood banking is performed (Helsedirektoratet, 2011). It is a very demanding and time consuming process. Blood is normally supplied from a blood bank and separated into three components: red blood cells, plasma and platelets.

The storing time is very different for the three components. Platelets require storage at 20-24 ° C and continuous agitation. They only have a shelf-life of five to seven days and only mature military theatres, where specialized blood bank facilities and reliable logistical lines are open, have the ability to establish blood banking capabilities for platelets. Plasma, on the other hand is supplied as a frozen product which needs to be maintained below -20 ° C during storage. It requires special shipping, and before use it must be thawed and

refrigerated. The red blood cells can be stored up to six weeks and requires constant refrigeration during storage and shipment (respectively in 1-6 and 1-10 ° C).

As mentioned above, the quality of the blood products declines rapidly, but there are also other challenges involved in blood banking. Viral and bacterial contaminations of the donor's blood can be transmitted to the patient. HIV and hepatitis are two examples. Therefore the blood has to be screened for infections before it is donated. There is also a risk of giving the wrong type of blood to the patient. A systematic logistical system, and meticulous typing and matching of blood between donor and recipient prior to transfusion are very important. There are many other important aspects to ordinary blood transfusion, but this is left out of in lack of space, and it is not necessary for understanding the concept of buddy transfusion.

2.1.2 Whole blood

Whole blood is when the donated unit of blood remains unprocessed after donation (except an anticoagulant which is added during the collection process to prevent coagulation of the blood in the bag). The storage time for whole blood is much less than components (Wilsher et.al, 2008). Recently, especially in Iraq and Afghanistan, there has been revealed some distinct advantages connected with the use of warm fresh whole blood (WFWB) during resuscitation of trauma patients (Spinella et.al., 2008). Particularly during situations in extreme and austere environments the WFWB has been favorable. In the far forward lines, the WFWB may be the only alternative. It could be a very useful resource in both pre-hospital and in Role 2/3 (surgical facilities along the lines of evacuation) settings, where ordinary blood bank resources are very limited. The only way of making blood available in these settings is through buddy transfusion.

2.1.3 Buddy transfusion

Blood can be made available in the far forward lines by the use of the principles referred to as *buddy transfusion* and *walking blood bank*. Buddy transfusion is when soldiers donate

blood to each other when the blood is needed, i.e. immediately after a combat casualty. All the soldiers in the patrol/platoon/etc are then considered a walking blood bank. Another option is to donate blood immediately before a mission by non-combating personnel (staff, technicians etc.). The blood will then be brought forward to the casualties and given to those in need. In these situations there is no time for blood typing and matching. The soldier's blood type has to be known in advance. The blood type is matched between donor and recipient. If that is not possible, type O can be used as a universal donor.

In both these scenarios it is impracticable to test the blood for diseases or contamination to the same extent that it would have been in a regular blood bank. This practice will have to involve testing of every deploying soldier for the same diseases that the regular blood banks do before taking in a new donor (i.e. HIV, hepatitis B and C etc). Herein lays a challenge facing the regular forces with regards to testing, but also in maintaining the soldiers' health. This aim might be easier to uphold amongst the SOF than with the conscripts and regular forces. Mainly because it is usually a much smaller force that is deployed, consisting merely of professional soldiers who have been through a strict selection process in advance. Still, this is only an estimated guess from my point of view and should be further explored in order to be a stated fact.

Why is buddy transfusion not used more frequently in the field? It has surely been done before (Kendrick, 1964). The concept is well proven and was used in both World Wars and during the war in Korea. The reason can be that there has been very little research on fresh whole blood after the component therapy was introduced after WW2. Today's technologies have discovered new ways of making the buddy transfusion safer: screening and pathogen reduction are two of them. So why do we not use this procedure more extensively? Why are we not rediscovering old ways in a new world? Is it because we do not know enough about the effects it may have on the donor? It has been assumed on a general basis that after the donation of one unit of blood (450 ml), the physical capacity of the donor is temporary reduced.

Fresh whole blood infusion can also be a potentially lifesaving intervention in situations where the casualties face long evacuation time or delayed transport. The casualties in shock

will respond positively to a resuscitation fluid that is warm and has a maximal oxygen carrying capacity in addition to the hemostatic function. There are also strong indications that WFWB is associated with improved survival for patients with combat-related traumatic injuries. Improved survival with partially fresh warm blood use, compared to stored components is reported by Spinella and others (Spinella et.al, 2008), who also concludes that the risk benefit ratio for patients with life-threatening haemorrhage who receives WFWB transfusion favors its use.

There are few reports which explore the aspects of donor safety, and in particular how donor combat readiness skills are affected immediately after donation. There has recently been a study that looks at the effects of donation of one unit of blood (450 ml) on physical performance and shooting skills among active duty soldiers in Norway (the study is described later, in sub chapter 2.1.8. However, the study does not include any prospective effects a donation might have on the stroke volume (SV) of the donor.

2.1.4 Exercise physiology

Regular exercise makes the cardiac system much more efficient in pumping blood and delivering oxygen to the muscles. During exercise, the SV, systolic blood pressure, cardiac output and mean arterial blood pressure increases and the blood flow to the muscles increase up to 80-85 % (Levick, 2003). The HR increases in direct proportion to the intensity of the exercise until the maximum HR is reached. The SV also increases proportionally with the exercise, usually 40-60% of maximal capacity until it reaches a plateau. Until the point of exhaustion it will remain unchanged. Initially after onset of exercise, there is a rapid rise in systolic blood pressure (BP) from the resting level. After this rapid rise, the systolic BP increases linearly with exercise intensity. The diastolic pressure however, remains stable or decreases slightly at the higher exercise levels. The BP responses are similar in both sedentary and endurance-trained subjects (McArdle D. et.al, 2001, p.319).

When we exercise, the cardiovascular system facilitates for the working muscles to be supplied with the increasing amount of oxygen they require. Both the heart rate and the SV are affected by this, as well as the cardiac output, blood flow, blood pressure and the blood

itself. The most important of these changes is the increase in cardiac output (CO)¹. The CO rises practically linearly with the rate of the muscles consumption of oxygen, which is a direct result of increased HR and SV. The increasing CO is mainly channeled to the active muscles and the heart (to the muscles up to 85% versus 15-20% at rest (Levick, 2003)). In sedentary males aged 20-25 years, CO during maximal exercise increases to an average maximum of 20-22 L · min⁻¹. The maximal HR for the same group averages at 195 beats · minute⁻¹. This leads the SV to generally range between 103 and 113 mL. The contrast is world-class endurance athletes who achieve a maximum CO of 35-40 L · min⁻¹. Below is a summary of the average values of the different mechanisms for both endurance-trained and untrained men:

At rest

	Cardiac output =	Heart rate X	Stroke volume
Untrained	5000 mL · min ⁻¹	70 beats · min ⁻¹	71 mL
Trained	5000 mL · min ⁻¹	50 beats · min ⁻¹	100 mL

Fig. 1.1 (McArdle, 2001, p. 347)

At maximum exercise

	Cardiac output =	Heart rate X	Stroke volume
Untrained	22,0 mL	195 beats · min ⁻¹	113 mL
Trained	35,0 mL	195 beats · min ⁻¹	179 mL

Fig. 1.2 (McArdle, 2001, p. 347)

¹ The volume of blood pumped by each ventricle per minute (not total output pumped by both ventricles (Vander, 2001, p. 747)).

2.1.5 Stroke volume

The stroke volume (SV) is the volume of blood ejected by a ventricle during one heartbeat (Vander, 2001, p.771). Under steady-state conditions the SV and HR, including the factors that alter the two determinants has effect on both the left and the right side of the heart. However, the two does not necessarily change in the same direction. In most exercise both SV and HR increases. Following a blood loss, the SV decreases while the HR increases. (Vander, 2001, p. 400). When we bleed, the blood volume in the body decreases. This leads to a reduced SV because when there is less blood to enter the heart, there is also less blood to exit the heart in every beat (Convertino et.al, 2006). The reduced blood volume leads to a reduced filling pressure of the heart, and through the Starling mechanism this leads to decreased SV.

Sub-maximal exercise for duration longer than 15 minutes causes a reduction in SV. This is because of the loss of water due to fluid shift from plasma to tissues, redistribution from the core to the periphery for cooling off the body and some is lost by sweating. The reduced SV then initiates an increase in HR to compensate. This is to maintain an almost constant CO as the exercise progresses (McArdle et.al., 2001, p. 348). The maximum SV usually occurs at 40-50% of VO_2 max which is correlates with a HR of 110-120 beats $\cdot \text{min}^{-1}$ in young adults (McArdle et.al., 2001, p. 473).

2.1.6 Donation of blood

When donating blood, the amount that is drained from the body is 450 ml (one unit). This is equivalent to 8-10% of the donors total blood volume (Norges Røde Kors Blodprogram, 2007, p. 8). When this amount of blood is donated, there are usually small, if any changes in vital signs (in a resting person). Before donating blood, every applicant is tested thoroughly to minimize the risks of complications with both the recipient and the donator. A questionnaire needs to be filled out and a blood test must be taken. Questions of relevance are: where you have vacationed or lived recently (outside of Norway), if you have been ill lately, any new tattoos and piercings must be reported and if you have changed sexual

partner recently you must inform the blood bank about this (Norges Røde Kors Blodprogram, 2007, p.4).

Before each donation a small amount of blood is drained and used to test for haemoglobin, ABO- and Rh (D)-typing, HIV and hepatitis B and C. Sometimes it is also tested for Syphilis, HTLV 1 and 2 (a viral disease which transmits via blood) and Ferritin (amount of iron in the blood). By completing all these tests, the risk of infecting the recipient is minimal and it is also very rare that serious side effects occur (Norges Røde Kors Blodprogram, 2007, p.5).

2.1.7 Findings from earlier studies

In 2010, Dan Gordon et.al. wrote a paper with the title: *Influence of blood donation on oxygen uptake kinetics during moderate and heavy intensity cycle exercise*. They wanted to assess the effects of blood donation on on-transient oxygen uptake kinetics during both heavy and moderate exercise (Gordon et.al, 2010, p. 298). By doing so, they wanted to examine the role of a cardiovascular control in the form of heart rate and pressures in both conditions.

The study showed that the oxygen on-transient kinetics is not affected by a 7, 9 % reduction in haemoglobin concentration of the blood. In the cardiovascular changes during exercise, they made some interesting findings: both in the bled and un-bled trials the heart rate attained were almost identical, even during heavy exercise. Gordon et.al. therefore suggests that it is reasonable to assume that the heart rate increment is achieved by a central sympathetic drive (Gordon et.al., 2010, p. 301). Also, in the bled state, the increase in pulse pressure is significantly greater. This study, in addition to two other similar ones, suggest that at sub-maximal exercise rates, the oxygen onset kinetics in phase 1 and 2 of the responses to stepwise changes in work load are unaffected by the oxygen carrying capacity of the blood (Gordon et.al., 2010, p. 302).

In 2006 Burnley et.al conducted a study, *Influence of blood donation on O_2 uptake on-kinetics, peak O_2 uptake and time to exhaustion during severe-intensity cycle exercise in humans*, with the hypotheses that: with the withdrawal of approximately 450 ml of blood, the reduction in oxygen carrying capacity this would ensue, might result in slower phase II O_2 uptake ($\dot{V}O_2$) kinetics, a lower $\dot{V}O_2$ peak and a reduced time until exhaustion during severe-intensity cycle exercise (Burnley et.al., 2006, p. 499).

The tests showed that the haemoglobin concentration was significantly reduced after the withdrawal of the approximately 450 ml of blood. $\dot{V}O_2$ peak and time to exhaustion was also significantly reduced. Also, the magnitude of the $\dot{V}O_2$ slow component was significantly reduced following blood donation owing to the lower peak attained (Burnley et.al., 2006, p. 502). However, the fundamental $\dot{V}O_2$ response's kinetic parameters, including the phase II time constant were not altered by blood withdrawal. In their article Burnley et.al conclude that a reduction in the blood's oxygen carrying capacity will result in a significant reduction in $\dot{V}O_2$ peak and tolerance in exercise. Still, it has no effect on the fundamental phase of the $\dot{V}O_2$ on-kinetics during severe-intensity exercise (Burnley et.al., 2006, p. 506).

In 2010, Geir Strandenes et.al. carried out the study: *Donor performance of combat readiness skills are maintained immediately after whole blood donation*. This study had its aim at supporting the development of a pre-hospital warm fresh whole blood programme. The main objective was to explore the effects a donation of blood would have on the donor's physical and combat related performance. The subjects were active duty soldiers who were above average fit. The study was able to conclude that buddy transfusion was safe and feasible for healthy, well trained soldiers and it did not decrease their combat performance.

The results showed that there was no significant decrease in physical performance after the blood donation. The HR-max were unchanged, max lactate levels showed no change in the results before and after the donation. However, there was a small, non-significant decrease in estimated maximal oxygen consumption. They also pointed out that on a special operations soldier; the donation of a unit of blood did not reduce his physical performance or combat skills. Still, the study stresses the fact that the tests were performed under ideal conditions and that the results cannot be compared to strenuous field conditions.

2.1.8 Physical requirements in a hostile environment

”You fight as you train. That is why you must train as you intend to fight” (Hæren, 2005, p. 18). It is a demanding task to participate in international operations. A soldier needs to be both versatile and athletic. He must be strong both mentally and physically to operate in the diverse environments that the military does (FFOD, 2007). The demands facing the soldier are very much unlike the ones facing for instance a cross-country skier. Cadet Sveinung Voreland wrote in his bachelor thesis from 2010 that the specific work requirements for a soldier today are: good aerobic and anaerobic stamina in addition to maximal and enduring strength (Voreland, 2010, p. 7). He must be in such a physical fitness standard that he is able to achieve the mental surplus it takes to consecutively make life or death decisions.

The intensity of the activities a soldier endures is diverse. It is often a strenuous and long lasting endurance activity. Still, it can also be a short, maximal performance i.e. suddenly a contact with enemy forces. He also needs good strength when he, for instance, is on a patrol and has to go down on his knees to secure in his sector several times with a lot of heavy kit on. This is one of the reasons why the soldiers need to be as versatile as he is. It would not help him much to perfect his performance in just one discipline, as the cross-country skier can.

3. Methodology

3.1 Method

The purpose of this pilot study is to find out more about the effects donating blood may have on the part that donates it. To narrow down the topic, I have directed my focus towards the SV and what effects exercising immediately after donation may have on it. In addition to exploring the physiological effects this might have on the human body, I have also tried to shed some light on the issues concerning practical use of blood transfusion/donation in the military setting, and discuss its feasibility.

The study in this paper is a pilot study and is based on the natural sciences. An experiment has been carried out in order to collect the quantitative data, enabling me to answer my thesis statement. The thesis statement has not been formulated into a testable hypothesis, but is instead as an open statement. The selection of population was a non-probability selection and convenience was a main criterion for selecting the test persons. The selection process to get participants for the testing was made up of volunteer soldiers from a medical course held for the medics from FSK/HJK² in the same period of time as the experiment. The risk of using this selection method is that the group that will be tested may deviate from the total population (i.e. the Norwegian Armed Forces). Because of the strict entrance requirements (physical and psychological) and the daily duty of the FSK it is reasonable to assume that they are in a higher physical shape than large parts of the rest of the Army³.

² Forsvarets Spesialkommando/Hærens Jegerkommando

³ Sindre M. Dyrstad writes in his doctor's degree that among the young men who complete their initial service in the Norwegian Armed Forces, the physical fitness has declined from 1980 and until 2002. Still, this does not necessarily have to create any consequences for the military since they have the possibility to select their serving soldiers (Dyrstad, 2006, p. 78).

3.2 Possible sources of error

3.2.1 Selection

A weakness with this study is that the size of the test group is very small ($n=2$). If I would have had a bigger test group the results would be more reliable. I could then have ruled out some results that might have been individual results. I would also have been able to get more credible results since the test would have been performed on a larger population. Still, the two subjects I tested were healthy young men with an irreproachable physical fitness standard. In addition, this paper is merely a bachelor's degree and it is not within the scope of this project to do the entire testing needed to draw statistical significant conclusion on this theme.

3.2.2 Instruments

One of the instruments used during the test, the Finometer® (Finapres Medical Systems, Amsterdam, Netherlands), are initially made for measurements made when lying flat or sitting still while being measured. It is not made for moving around and sweating on an ergometer cycle. Despite this, with some minor alterations, the equipment worked as expected. It was not until the second testing and the last push that there were some complications with the Finometer, but the measurements from the rest of the equipment used enabled us to calculate the numbers manually. Besides the minor problem with the Finometer at the end, the instruments showed stable and reliable results throughout the testing

3.3 Experiment

The study was carried out in a laboratory designed for cardiovascular and thermoregulatory research. This was a pilot study, and thus no formal application was sent to the Regional Ethics Committee. Still, an informed consent was obtained from the participants. A medical doctor and researcher were present and led the project.

3.3.1 Subjects

Two healthy non-smoking male volunteers who also did not use the substance snus (Swedish chewing tobacco) accepted to participate in the study. Both were 24 yrs old, height 182 ± 1 cm, weight 72 ± 4 kg, BMI 21.7 ± 1.0 kg/m². On the day of each experiment they were instructed not to exercise, drink caffeinated beverages or eat within 2 hours prior to the experiment. The subjects were dressed in t-shirt and shorts. They did not receive anything to drink during the experiments.

3.3.2 Experimental protocol

The subjects performed a graded exercise test twice, before and immediately after donating 450 ml blood. The exercise test was performed on a stationary bike. Depending on the subject's estimated physical fitness, the exercise was graded individually in three stages, going from low to high resistance. The increase was linear: 75-150-225 watts.

3.3.3 Measurements

The subjects had a 3-lead ECG connected. Arterial blood pressure wave (ABP) and Stroke volume (SV) was measured on the right hand 3rd finger (Finometer). Data from HR and SV were fed online to a personal computer, where it was displayed real-time, and stored for later analyses. In addition we asked for, and noted, anthropometric variables.

3.3.4 Data analysis and statistics

No statistics were calculated (n=2). Data was noted on an Excel sheet.

3.4 Collection of data

Heart rate: is measured from EKG (electrocardiogram). Every test person is connected to an EKG-machine that can write out curves on a strip of paper. Simultaneously the signal is

transferred to a computer which automatically and continuously calculates the number of heartbeats per minute by measuring the time between every R-point.

Arterial blood pressure: was measured towards the end of each working period using the Finometer.

Ventilation: is registered by the test person breathing into a mask which covers both nose and mouth. This is equipped with a 3-way ventilator which ensures that the inhalation and exhalation happens through each separate opening. There is installed a flow-meter on the inhalation-side. This generates an electric signal which is transferred to a computer with a programme that, for each respiration cycle, calculates: Tidal volume, frequency and ventilation. It is difficult to put the mask on and off so it should remain on for the duration of the experiment.

O₂-analysis: Tests of mixed exhalation gas (from the other side of the ventilator) is collected in a plastic bag at the end of each work period. The collected gas is then analyzed of/ for O₂ content. The analysis is performed by an instrument that exploits the paramagnetic qualities of the oxygen. Measurements of the ventilation and the O₂-fraction in mixed exhalation gas can be used to calculate the oxygen uptake.

4. Results

The main finding from subject number one is that there is a decrease in SV immediately after donating 450 mL blood. The results are shown in the table below. Post-donation, for each level of work load on the bicycle, there was a decrease in SV and a correlating increase in HR. The systolic BP decreased and the diastolic BP increased. In both pre and post donation test, the Mean Arterial Blood Pressure increased.

Table 1 shows the results for cyclist number one using the Finometer: From left to right

Pre donation:

Work Load	SV	SBP	DBP	MAP	HR	CO-finometer	CO-calc
75	79	164	63	97	123	8	10
150	89	152	97	115	144	13	13
225	94	183	111	135	170	16	16

Post donation:

Work load	SV	SBP	DBP	MAP	HR	CO-finometer	CO-calc
75	68	139	99	112	124	9,01	8
150	78	142	94	110	156	11,7	12
225	75	165	108	127	181	14,5	14

Table 1 is showing, from left to right: work load on bicycle (watts), stroke volume (mL), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg), Mean Arterial Pressure (mmHg), Heart Rate (beats/min), Cardiac Output using Finometer (L/min), Cardiac Output Calculated

Table 2 list the measurements of ventilation for subject number 1. Included is also HR from the ECG device. HR is increased, as stated previously. The ventilation parameter varies, which is typical, but the overall oxygen consumption is approximately the same after donating 450 mL blood. In this table the SV is estimated based on the parameters measured, and one can also observe a tendency to a lesser stroke volume after donation.

Table 2

Pre-donation

Work load	Vent	Freq	HR	Tot.vent	O2-cons.	CO-estim	SV-estim
75,0	1,8	15,3	120,0	27,3	1,2	12,2	101,5
150,0	1,9	25,0	153,0	48,7	1,9	16,9	110,3
225,0	2,6	31,8	180,0	82,2	2,9	20,6	114,4

Post-donation

Work load	Vent	Freq	HR	Tot.vent	O2-cons.	CO-estim	SV-estim
75,0	1,3	26,2	134,0	34,3	1,4	12,9	96,6
150,0	2,0	26,9	154,0	52,0	2,0	17,0	110,7
225,0	2,7	34,3	194,0	92,8	2,9	20,7	106,5

Table 2 is showing, from left to right: work load (Watts), Tidal Ventilation (Liter), Ventilation frequency (min^{-1}), Total Ventilation (Litre/min), Estimated oxygen consumption (Litre), Estimated Cardiac Output (Litre/min), Estimated Stroke Volume (mL).

The second test was unsuccessful because of a malfunction in the equipment. Still, the results indicate that the reduced blood volume has an effect on the physiology of an exercising soldier.

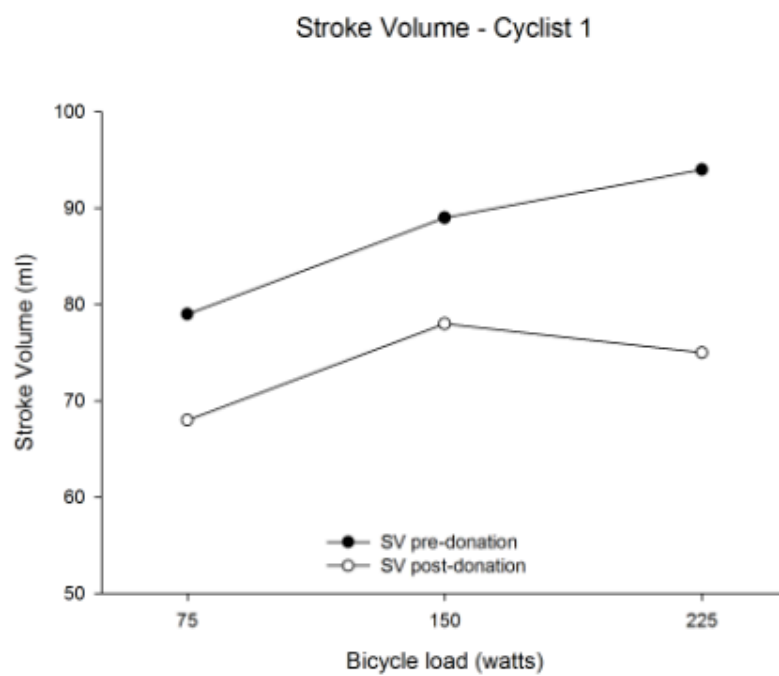


Figure 1.3: shows a graphic representation of cyclist number one's stroke volume pre and post donation.

5. Discussion

5.1 General

Since this was a pilot study, there is no statistical power in these results. The aim of the study is to be able to generate a hypothesis for a larger clinical study. To our knowledge, no one has ever used a Finometer to measure SV during exercise before, and figuring out how to do it was also an important part of the study. The technique we came up with was not flawless and it resulted in one successful and one unsuccessful experiment. For when the larger clinical study will be executed, the technique must be improved so that no results will be lost on account of a misreading.

In addition, the physical fitness shape of the two tested men was above average. This could influence the results since they would be better fitted to endure a blood loss, even of such a small amount. Since they are in the higher stratum of the physical shape of the population, it may affect how they respond to the test-situation, i.e. draining 450 ml of blood and immediately afterwards start exercising on an ergometer cycle. Since this study takes aim at uncovering the safety aspects with regards to the Special operations forces, it should not have any relevance for the results. However, this important aspect must be taken into consideration if buddy transfusion were to be introduced to the armed forces in general.

In this context it must also be mentioned that the aim here is not to question the general military transfusion guidelines or policies, nor to promote the use of whole blood as a general replacement for blood component therapy. The goal is rather to improve the availability and quality of blood for the SOFs when they operate in the austere environments that they often do.

5.1.1 Measuring stroke volume during exercise

Measuring SV non-invasively during exercise is difficult. It is almost impossible with pulsed ultrasound-Doppler, and the finger-plethysmograph method is probably the best. To be able to get correct readings, there has to be no motion in the hand and fingers of the arm where the measurements are made. This was solved by using a bandage rubber band to fasten the finger-plethysmograph device to the lower arm. A lesson learned was also that the subject should have an opportunity to sit/lay down while donation. The attached technical devices must then be fastened in a way that they do not have to be detached when this happens. A semi-supine bicycle might be better, but one needs to be aware that this might change SV physiology.

5.1.2 Decreased stroke volume

During the post-donation pushes, the SV decreased. To compensate for this, the heart rate increased. This was not a surprising result since this is how the physiology functions during a blood loss. However, as mentioned in sub-chapter 2.1.6, the SV also have a tendency to decrease when exercising sub-maximally for durations of more than 15 minutes. This might have had an influence on the results from the experiment since the test lasted for approximately 45 minutes. The fluid shift within the body may have affected the results from the experiment to a certain degree.

But does this reduction in SV have any significance when it comes to survival during a military operation? Yes is the answer to the latter question. If a soldier were to be shot immediately after a buddy transfusion conducted in the field to save a platoon member, it would probably have a negative effect on the donor. This is because his body is already compensating for a recent blood loss. An injury which would lead to a blood loss of e.g. another 450 ml would suddenly be doubled, and the physiological reactions would be more serious than if he were shot before donating blood. The sudden increase in blood loss might result in tachycardia⁴, weaker peripheral pulses and he might act confused and irritable. In

⁴ “Relatively rapid heart action whether physiological (as after exercise) or pathological” (web 2).

this way a fairly small and insignificant injury might double in effect when experienced after a donation of blood.

The recovery time after a donation and until blood volume is fully restored is within a few hours under ideal conditions (web1). Drinking lots of fluids post donation reduces the recovery time. However, if the military setting is in a warm environment such as during an operation in for instance Afghanistan, the temperature would be a contributing factor to the prolonging of the recovery time for the soldier who has donated blood.

5.1.3 Max VO₂

There would be great interest in performing a similar experiment with a result from a VO₂ test. It is the results from such a study that would be the most interesting and relevant to us. However, it is impracticable to perform a test of the maximal performance immediately after a donation of blood, because the subjects need too much time to reconstitute in order to perform the same as before the donation. For the test subjects to be restored enough to produce a maximal yield again, they need a couple of days. By then the factors will have changed too much to obtain any valid results.

What could we have concluded from a prospective maximal strain test? Based on the results that Burnley et.al. found in their study; a reduction in the blood's oxygen carrying capacity will result in a significant reduction in VO₂ peak and tolerance in exercise, but how would the SV react under such conditions? How would it react to an increasing HR and a further decrease in blood volume due to the shift of fluid from plasma to tissues and the redistribution in order to cool off the body? According to the human physiology, the SV will continue to decrease until the patient will suffer from among others, hypotension⁵. But how often are soldiers exposed to conditions similar of a maximal strain test? Most military activities are carried out mainly in the sub-maximal level, with elements of maximal strain levels. An example of this variation will be during an enemy contact, which is also most likely the situation where a soldier might have given a buddy transfusion.

⁵ "Abnormally low pressure of the blood—called also *low blood pressure*" (web 3).

The tests made by Burnley et.al. showed a significant reduction in VO_2 peak and time to exhaustion 24 hours after donating blood. The question that arises is: why do the results from the Bergen-study⁶ show that the soldier's performance was unaffected by a blood loss of 450 ml? All the test results show that the soldiers performed as well or even slightly better in the trials post donation. One reason for these results may be because of the Hawthorne effect⁷ but more importantly, what this also may indicate is that the motivational factor is just as important as the physiological one. It seems as if a placebo effect may be desirable. If the soldier does not think of the blood loss as a confining factor, it will not hinder him either. The mind set of the soldier is just as important as the minor physiological changes within him.

Due to the general demands that are required of a soldier, he will have no problems performing as at the same level as before the donation. Motivation is the key factor here. The physiological changes for the soldier will be minor and therefore not noticeable. A top athlete such as Marit Bjørgen might experience a slight difference in her post performance, but that is because she spends years making perfect her performance within that one special sport. The soldier however, is more like a generalist and is trained to perform in more than one "exercise", these mostly at a sub-maximal level and over time.

5.1.4 Blood

The principle of buddy transfusion is in a way limiting in itself since the humans are the blood bank. This involves the soldiers being at good health and that they be kept that way. Deployment is in a way a possibility to freeze time. The way international operations are today there is no possibility for a social life outside the military arena. During a deployment the most potent threat is if the unit is stationed in an area where diseases such as e.g. malaria and the West Nile virus are present. Despite this it is still a lot easier to have a general view

⁶ Geir Strandenes et.al. *Donor performance of combat readiness skills are maintained immediately after whole blood donation.*

⁷ The Hawthorne effect: "the alteration of behaviour by the subjects of a study due to their awareness of being observed" (web 4).

of the soldiers' health regarding human blood banking during deployment than while serving at home. When the soldiers are at home it is much more challenging to maintain control of who is a source of infections and who is not. It may also become a very demanding task to keep a platoon infectious-free. This will involve strict routines before each new deployment in order to make every soldier (SOF soldier) a walking blood bank before he deploys again. After deployment the soldiers would have to refrain from having sex with a new partner, avoid contact with needles etc. for the duration of their deployment in order to stay infectious-free and eligible for donation.

It should be an objective to create a solidarity within the e.g. platoon which would take care of the soldiers attitude towards being a walking blood bank and the responsibility that follows. This solidarity could create a setting where it is not accepted to be the one in the team or platoon who cannot give blood to save one of the others. This way every soldier would be encouraged to stay infectious-free. Because of the possibility of viral and bacterial contamination of the recipient's blood, there needs to be strict regulations as to who may be eligible to function as a blood bank and who may not. Another factor that needs to be taken into consideration is how strict the regulations should be.

If the principle of buddy transfusion will be a practice, there are some precautions that can be done in order to further the blood transfusion safety. Before donating blood, the medic could have a form very much alike the one you fill out at the blood bank the first time you go there to give blood. This form would have to be modified in order to better suit the military standards. In that way the medic can rule out that the soldier has been in a situation recently that will make him unfit to donate blood. Another precaution that could be made is the use of quick-tests. The operative environment and the logistical challenges does not always make possible the same, thorough testing as the Norwegian blood bank performs on each specimen of blood. Something similar but simpler must be used in order to ensure that the most dangerous infections are not present and that the blood types are matching.

6. Conclusion

What the experiment was able to demonstrate is that during graded exercise post donation of one unit of blood, the SV decreased significantly in both test subjects. It is also reasonable to say that the experiment showed how a reduction in SV (because of a conducted buddy transfusion) will play a negative part when a soldier is injured during e.g. battle. The already reduced SV may be doubled in effect. However, the risk of a subsequent injury set aside, the donation of blood would have no significant effect on the soldier's performance in combat readiness skills. It seems as if the psychological factor is just as important as the physiological attributes in this context. If the Norwegian armed forces were to introduce buddy transfusion, strict routines would have to be introduced before every deployment. To maximize the transfusion safety, the Norwegian armed forces could develop routines similar to the ones used by the Norwegian blood bank. Solidarity amongst the soldiers towards staying infectious-free for the duration of the deployment is of great importance.

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Attachment

Remarks

Application to the Regional Ethics Committee

This study was merely a pilot project with a very small test group ($n=2$). Because of this, no formal application was sent to the Regional Ethics Committee.

Informed consent from the participants

An informed consent was obtained from the participants. The written consent is located at Rena with the medical doctor who participated in the study. These can be acquired at request directed to me, Kritin Stormyr Skogen.

Leading the project

A medical doctor and researcher (Erling Bakkestad Rein) were present during the experiment and he also had the lead of the project